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## ON HEREDITARY EPILEPSY.

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ON THE

## SEAT OF VASO-MOTOR CENTRES.

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OF NEW YORK.

REPRINTED FROM THE

TRANSACTIONS OF THE AMERICAN NEUROLOGICAL ASSOCIATION

VOL. II., 1877.

126

NEW YORK

G. P. PUTNAM'S SONS

182 FIFTH AVENUE

1877



## ON HEREDITARY EPILEPSY.

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BY EUGENE DUPUY, M.D., OF NEW YORK.

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IT is well known that Dr. Brown-Séquard, in the course of his magnificent researches into the nature of epilepsy, has discovered that that malady, artificially induced in the guinea pig, is in rare instances transmitted to the young.

That question of heredity—one of the most interesting, of paramount practical importance—has for some years past occupied my mind. I have endeavored to find to what extent the disease is hereditary in the guinea pig, for it is known that although an epileptic person is very rarely descended from an epileptic parent, yet epilepsy is very certainly an hereditary malady. I do not believe that Dr. Brown-Séquard has seen more than thirteen or fifteen cases of epilepsy in the young of guinea pigs which had been artificially made epileptic. If it is considered that that eminent physiologist has had under observation, in the course of twenty years, certainly more than a couple of thousand animals, it will be seen at once that in the case of epilepsy the reverse is obtained of what is observed with regard to lesions of the sympathetic nerves or corpora restiformia, which lesions are in all cases hereditarily transmitted, in those animals.

I am aware that Obersteiner, of Vienna, has published facts which will go further to show that the ratio of inheritance is both greater and more subject to certain laws than Brown-Séquard, and myself independently, have been able to ascertain. But how to explain the difference between the results of Obersteiner on the one hand, and Dr. Brown-Séquard's and my own on the other, I am at a loss just now. It is well known that when a lesion is made to the spinal cord, to the medulla oblongata, to the brain, to the sciatic nerve of a guinea pig, which animal has never been found to suffer from idiopathic epilepsy, after the lapse of

three to ten weeks a disease develops itself, which has all the characteristics of epilepsy in man. That disease ushers itself by the following phenomena: First, a few days after the operation, whether made on the cerebro-spinal centres, or the sciatic nerve, it is found that an area of skin on the same side with the seat of the lesion, and which is circumscribed by the limit of innervation of the trigeminus and the first cervical posterior nerves, by degrees loses certain faculties and acquires new ones. The sensations of pressure, of pain, of cold, heat, electricity, etc., are all benumbed and ultimately disappear; the faculty of feeling tactile impressions alone survives, and on that account appears even augmented.

It is observed that tickling this zone at first gives rise to involuntary twitchings in the muscles of the jaw, then of the eyes, and of the nose, on the same side; by degrees those twitchings become more strong and more general; then they manifest themselves on the other side also, and after a few weeks the animal has regular convulsions after each tickling of the zone, which lastly culminate into a genuine attack of epilepsy. That epilepsy I will not describe, because it is already well known to all; suffice it to say that it represents the typical "grand mal," even to the consecutive stupor and insanity sometimes observed in the human species. It happens, however, that a guinea pig will sometimes recover from the vice spontaneously, and when this does occur the following remarkable phenomena are noticed: the hair of the epileptogenic zone falls off; all the lost faculties return by degrees; the animal by degrees also ceases to have, first, attacks of epilepsy and then general convulsions, afterward twitchings, etc.; in a word, all the phenomena recur in the reverse order.

The explanation of these facts may be found in this circumstance: that the different operations made upon the nervous elements of the animals determine in them a process of inflammation, of which each stage is characterized by a corresponding series of convulsive phenomena of different degrees of severity, and that when the irritation having run its course, or the inflammation rather, the tissues become healthy again, then the disease to which it gave rise disappears; at all events, in the case of section or other disorder of the sciatic nerve, it has been ascertained that there is such a relation between the two processes, which fact is beautifully illustrated in the instance where the nerve has been simply divided.

Guinea pigs, which have become epileptic after a lesion of the cerebro-spinal centres, have no outward symptoms or peculiarities save the epileptogen zone during the existence of the disease. But when the malady has been consequent upon lesion of the sciatic nerve, it happens that the two outward toes of the posterior leg, which are innervated by the sciatic nerve, become anaesthetic, and being moreover paralyzed, drag on the floor, very soon become congested, the skin tears off, and as soon as blood has shown itself, the animal furiously bites at the parts and eats them until he reaches the limit where sensation is still preserved; he then takes care to protect the raw surfaces, which accordingly heal entirely; so that at last the animal has a leg terminated by one toe alone.

When young are born of epileptic guinea pigs which have suffered lesions of the cerebro-spinal centres, these young present all the phenomena present in the parents and in the same order; but when the parent has had a lesion of the sciatic nerve, the young *which is to become epileptic* is born with only one toe to the posterior leg, or two or three supernumerary toes, holding to the limb by a very tiny pedicle.

In all cases, the young are not born epileptic, but after six or seven weeks they begin to manifest the symptoms in the same order, as to manifestation and time, as the parent which was operated upon. I repeat that such occurrences of inheritance are very rare; but I must add that I have seen the vice transmitted through five generations, which amounts to about twenty animals in all; out of these only three lived to become <sup>completely</sup> epileptic, and all those which developed epilepsy were not born of epileptic parents, but of parents which were born of epileptic ancestry. I have not been able to go further than this. I must state that frequent examinations of the sciatic nerves of such offspring as were epileptic or born toeless, have satisfied me that at no time, either before, during, or after the entire development of the disease, was there anything to be discovered in the nerve, of an abnormal nature, as I have had some which were killed at each of those periods. All the animals I had had become epileptic after lesions of the sciatic nerve. It becomes evident therefore that, as Dr. Brown-Séquard has himself pointed out, it is not a disease which is inherited, but a power to develop a whole morbid process.

How is the process brought about, or what is the physiological rationale of these phenomena?

I deem it necessary to enter into some facts of embryology here, as it will be not only the single way of giving a plausible account of the facts, but also to surmise the most justifiable mode of treatment in cases where the outbreak of this disease can be feared.

It is well known now that two cells in the female system concur to the formation of the embryo : the one known under the name of germinative cell, and the one described by Balbiani. These two cells have very different significations: the first one only develops itself in the adult female, whilst the second one is found to represent atavie activity, as it pre-exists the other; when, however, the fecundation has taken place by the agency of Balbiani's cell upon the other, which is nothing more than a nutritive storhouse, an independent organism is formed which goes through a period of independent existence, very soon to vanish into an ultimate period of retrogression, unless the male spermatozoa comes to fecundate a second time the new organism and thuswise allow of the development of a new being. The male spermatozoa being organisms resulting from a like process. There is, therefore, a double fecundation.

Now it becomes apparent that when the malady is inherited by those of the first generation the morbid element is entirely in the germinative cell, as it alone represents maternal influence, and as the process at that stage is a mere nutritive one, the view we must take of the vice is that it has acted upon, first, atavie element in Balbiani's cell, and the new organism thus formed and already tainted, when impregnated by the spermatozoa, also influences that organism, so that the new being is potentially epileptic; but when, on the contrary, the diseased animal is one descended from the young of an epileptic pair, which young was itself not epileptic, it becomes evident also that in that case the vice has been transmitted through Balbiani's cell, or its equivalent organism in the male spermatozoa.

I take the liberty of pointing out that what I have just said is something more than a mere theory, as the constituting facts upon which it is founded are amenable to rigid demonstrations.

The practical deductions to be drawn from those facts I trust are plain enough not to go into further details.

I hope to be able to bring some other interesting facts before the society at no very remote period if circumstances allow me to proceed in this very fascinating inquiry.

## ON THE SEAT OF VASO-MOTOR CENTRES.

BY EUGENE DUPUY, M.D., OF NEW YORK.

SINCE the localization of the cilio-spinal centre in the upper cervical portion of the spinal cord by Waller and Budge, physiologists have been very eager to localize a number of other vaso-motor centres in the cerebro-spinal axis. Some are of the opinion that there is one principal centre in the upper cervical cord and medulla oblongata, and minor ones lower in the axis of the cord; others, that the centres are met with all along the spinal cord, and can be found up to the base of the brain. Lately, however, Eulenberg and Landois have localized new vaso-motor centres in those areas of the cortex cerebri which are supposed by some to be psycho-motor centres.

Among several physiologists who have not accepted either of the different theories reported above, Chauveau and Claude Bernard are pre-eminent. Chauveau has proved experimentally one fact of very great importance with regard to the cilio-spinal centre: it is that the effects of lesions or irritations of that region of the upper spinal cord, as observed in the eyes, although manifested by the agency of that branch of the sympathetic which passes through the first cervical ganglions, yet are mere reflex actions started from the posterior columns of the spinal cord. Any one who will read his paper in Brown-Séqnard's *Journal de la Physiologie* can no longer entertain any doubts on that point.

Claude Bernard has proved also that vaso-motor nerves do not accompany all the spinal mixed nerves, and, moreover, that vaso-motor nerves become connected with the spinal roots only at that point where these roots make their exit from the spinal marrow and receive their sheathing of pia mater. François Franck lately demonstrated also that the same holds good with regard to the so-called cranial nerves.

Those three authors, however, have said nothing about the real origin of the vascular nerves. It is my object in this short communication to state the results which I have obtained from experiments conducted with a view of settling that problem.

One author has, as far back as 1845, tried to establish that the sympathetic nerves take their origin in the arachnoid. Ranney has published in the volume of the Medico-Chirurgical Transactions for that year a memoir and a plate to that effect. His views have been criticised by Henle and others.

If we consult writers on comparative anatomy we will see that the opinion of the most advanced authors is very aptly put forward in the following by Gegenbaur, who says of the sympathetic system :

Its principal ramifications, going to the nutritive apparatus (intestinal canal, vascular system, respiratory organs), as well as to the uro-genital apparatus, derive their origin from the ganglia, but receive fascicles of nerves from the cerebro-spinal nerves, which thus keep them in the dependence of the central organs.

It is rational to state that, as the older physiologists had it, the sympathetic system is independent of the cerebro-spinal system, if, as Bernard, François Franck, and Chauveau have proved, each in his way, the sympathetic has no *direct* connection with the cerebro-spinal centres.

I have undertaken a certain number of experiments which I believe afford reasons enough to accept the view that, instead of receiving nerves from the cerebro-spinal centres, the sympathetic sends fibres there.

Brown-Séquard, and also Vulpian, have demonstrated, the former that irritations of the kidneys or supra-renal capsules induce a contraction of the bloodvessels of the corresponding half of the spinal cord at the level of those organs : and the latter, that galvanic irritation of one of the communicating branches of the ganglionic chain in the abdomen also induces contraction of the bloodvessels in the spinal cord at the level of the irritation.

I have seen that when the spinal canal is opened in the length of two or three centimetres in a vigorous guinea pig, and profuse bleeding has been avoided, which is an easy thing to do with little habit of experimentation, the irritation of any of the fibres of the sympathetic, at a corresponding level with the exposed spinal cord, will bring on paleness of the spinal bloodvessels. In the guinea pig the sympathetic cord is admirably adapted

for such experiments, as all along the vertebral column, on both sides of the aorta, and at a little distance from the foramina of exit of spinal nerves, but on a line with them, ganglia are found which are disposed and connected in this manner: two opposite ganglia are connected together by a transverse bundle of fibres, and also each with its upper and lower fellow by a cord, so that there is a complete square or oblong, according to the size of the vertebra upon which it lies, and of which the four angles are ganglia. From those ganglia fibres can be followed, which, running around the body of the vertebra, reach the foramina, beyond which it becomes connected with the spinal ganglion. Irritation of any of these fibres by means of a very weak faradic current will bring on contraction of bloodvessels of a limited area of the corresponding half of the spinal cord.

Moreover, I have also seen that the distribution of those sympathetic fibres from the spinal ganglia to the two roots of nerves is unequal, inasmuch as there is a difference in effects observed according as irritation is practiced upon the posterior or the anterior roots. Irritation of the posterior roots has greater influence of inducing contraction of bloodvessels in the cord than that of the anterior roots. If an examination of the two roots is made after they have been sectioned in the immediate vicinity of the ganglia, a month after this operation, it is found that only a number of healthy fibres are found in the posterior root, whereas the greatest number of fibres are found healthy in the anterior root.

I believe that this fact, taken into consideration with the observations of Waller himself and his followers, together with the admirable investigations of Professor Ranvier, and those published later by Dr. Amidon of New York, and several other histologists, which have shown the existence of T-shaped fibres in the spinal ganglia, fibres which certainly belong to the sympathetic system—go a good way toward supporting the view which I have expressed, that the vaso-motor apparatus is entirely independent of the spino-cerebral centres.

Microscopic observations have shown me also that when the Wallerian method is applied to the study of that question, it is seen that degenerated fibres are found in the meshes of the pia mater on a level with the roots sectioned.

I have seen also that irritation of the spinal and cerebral pia mater at any level, but more at different levels, has very great power to contract spinal and cerebral bloodvessels.

Indeed, when the experiment is made on a strong healthy animal of laying bare the spinal canal in the lumbar region, or in the cervico-braehial, or the bulbar portion (this latter operation is very easy at the level of the oecipito-atloidian membrane in all mammifera), and care be taken to avoid hemorrhage and the irritative influence of atmospheric air, I have seen that *all* the vaso-motor symptoms observed by Brown-Séquard, by Schiff, and by their followers, after section or hemisection of the spinal cord, can be also observed by mere lesions of the pia mater.

The pia mater in the neighborhood of the upper medulla oblongata and pons is exceedingly rich in ganglionic corpuscles and fibres which penetrate into those centres either alone or along bloodvessels, as can be seen almost with the naked eye. The ehoridian membrane is specially rich in such elements; the pia mater over the so-called psycho-motor region also to a high degree.

I have made on rabbits, which are specially adapted on account of their faculty of feeling only intense pain, the following experiment, which proves, to some extent, that my view may be correct: If, when the Gasserian ganglion is exposed, irritation of the trigeminus beyond the ganglion gives rise to pain which the animal tries to avoid, but if, before irritating the nerve, the ganglion, which is found on the Gasserian ganglion, be destroyed, or if merely its fibres going to the centres be sectioned, then irritation of the nerve induces such pain that the animal moans in the most pitiful manner for some little time after, and in the same way that it does when the hind foot is pressed on the same side with the lateral half of the spinal cord sectioned as in Brown-Séquard's experiments on crossing of sensitive fibres. I will add, that irritation of the trunk of the trigeminus before the ganglion, taking care to avoid squeezing the vaso-motor nerves, by careful manipulation, will give confirmatory results.

These facts are few and not very convincing; but they carry evidence enough with them to allow us to discard the old theories, if not to accept this new one.

The bearing of those facts on infantile paralysis, myelitis, encephalitis, chorea, and other convulsive disorders, is very interesting and suggestive. As my object is merely to put forth the meagre results which I have thus far observed, I will not say more upon the subject just now, as I am still pursuing the experiments. But I must add that I cannot in any sense ascribe the facts

which I have observed to reflex actions through sensitive and sensory fibres, because I have been able to observe them also even when the animals experimented upon were so far under the influence of anaesthesia that reflex actions could no more be awakened through the agency of the sciatic nerve laid bare.

## HEREDITARY TRANSMISSION OF PECULIARITIES.\*

THIS was a report of a curious case of heredity. Dr. Dupuy stated that he owed to his friend, Dr. Gibney, the opportunity of observing a family consisting of father and mother, five children, and one grandchild. The father and mother are semi-ambidextrous. All of the children and the grandchild are ambidextrous to an annoying degree: all of the movements which they perform with one hand are simultaneously performed by the other hand. The girls are obliged to use only one hand when dressing themselves, or when cutting patterns, and hold the other hand down by their side, because the two hands perform the same movements at the same time, and would interfere with each other.

Attention was called to the fact that the father of the grandchild is not semi-ambidextrous. Dr. Dupuy has made experiments upon these persons, and has found that if the skin of the forearm on one side be kept well dry, and a rapidly interrupted electrical current be used, so as only to call forth reflex actions, it is possible to induce synchronous movements in the fingers of both hands, and also muscular contraction in the lumbricales muscles of the fingers, which are too rapid to be carried on by the will. Dr. Dupuy considered these facts of great interest when coupled with the facts which he reported yesterday about hereditary epilepsy.

\* From the Proceedings of Session of 1877, p. iv.



